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CLAIMS

We claim:

1. A method for suppressing tumor growth in an individual comprising: administering a target cell-specific adenovirus vector, said vector comprising an adenoviral gene essential for replication under transcriptional control of a target cell-specific-transcriptional regulatory element (TRE), and at least one antineoplastic agent in amounts sufficient to suppress tumor growth, wherein the amount of adenovirus vector and/or anitneoplastic agent administered is less than that known in the art to be effective for suppressing tumor growth when administered alone.

2. The method of claim 1, wherein the antineoplastic agent includes alkaloids, alkylating agents, antibiotics, antimetabolites, immunomodulators, nitrosoureas, hormone antagonists/agonists and analogs, or photosensitizing agents.

3. The method of claim 2, wherein alkaloids include docetaxel, etoposide, irinotecan, paclitaxel, vinblastine, or vincristine.

4. The method of claim 2, wherein alkylating agent includes cyclophosphamide, estramustine, ifosfamide, carboplatin, cisplatin, dacarbazine, or thiotepa.

5. The method of claim 2, wherein antibiotics include bleomycins, doxorubicin, epirubicin, mitomycins, mitoxantrone, or valrubicin.

6. The method of claim 2, wherein antimetabolites include edatrexate, methotrexate, 5-azacytidine, 5-fluorouracil, or gemcitabine.

7. The method of claim 2, wherein immunomodulators include interferon-alpha-2a.

8. The method of claim 2 wherein nitrosoureas include carmustine or lomustine.

9. The method of claim 2 wherein hormone antagonists/agonists and analogs include prednisone, taxmoxifen, exemestane, anastrazole, letrozole, goserelin, or leuprolide.

10. The method of claim 2 wherein photosensitizing agents include porfimer sodium.

11. The method of claim 1 wherein said target cell-specific TRE is specific for target cells including bladder, liver, prostate, breast, colorectal or melanoma cells.

12. The method of claim 11 wherein said target cell-specific TRE includes probasin (PB)-TRE; prostate-specific antigen (PSA)-TRE; mucin (*MUC1*)-TRE; α-fetoprotein (AFP)-TRE; *hKLK2*-TRE; tyrosinase-TRE; human uroplakin II-TRE (hUPII); carcinoembryonic antigen (CEA)-TRE; or cell status-specific-TRE.

13. The method of claim 11 wherein said TRE specific for liver cells is an AFP-TRE.

14. The method of claim 11 wherein said TRE specific for prostrate cells include PB-TRE; PSA-TRE; and *hKLK2* TRE.

15. The method of claim 11 wherein said TRE specific for breast cells include CEA-TRE and *MUC1*-TRE

16. The method of claim 11 wherein said TRE specific for colorectal cells is a CEA-TRE.

17. The method of claim 11 wherein said TRE specific for melanoma cells is a tyrosinase-TRE.

18. The method of claim 1 wherein said adenoviral gene essential for replication is an early gene.

19. The method of claim 1 wherein said adenoviral gene essential for replication is a late gene.

20. The method of claim 18 wherein said adenoviral gene essential for replication is E1A.

21. The method of claim 18 wherein said adenoviral gene essential for replication is E1B.

22. The method of claim 20 wherein E1A has a mutation in or deletion of its endogenous promoter.

23. The method of claim 21 wherein E1B has a mutation in or deletion of its endogenous promoter.

24. The method of claim 21 wherein E1B has a deletion of the 19-kDa region.

25. The method of claim 1, wherein the adenoviral vector comprises co-transcribed first and second genes under transcriptional control of a target cell-specific TRE wherein the second gene is under translational control of an IRES and wherein at least one of said first and said second genes is an adenovirus gene essential for replication.

26. The method of claim 1, wherein the TRE is specific for prostate cells and the antineoplastic agent includes antimetabolites, alkylating agents, antibiotics or

alkaloids.

27. The method of claim 26, wherein the TRE is specific for prostate cells and the antineoplastic agent includes doxorubicin, mitoxantrone, paclitaxel, docetaxel, etoposide, 5-fluorouracil, estramustine, or cisplatin.

28. The method of claim 27 wherein the TRE specific for prostate cells includes PB-TRE; PSA-TRE; or *hKLK2* TRE.

29. The method of claim 1, wherein the TRE is specific for liver cells and the antineoplastic agent includes antimetabolites, alkylating agents, antibiotics and alkaloids.

30. The method of claim 29, wherein the TRE is specific for liver cells and the antineoplastic agent includes doxorubicin, mitoxantrone, mitomycin C, paclitaxel, 5-azacytidine, gemcitabine, docetaxel, etoposide or cisplatin.

31. The method of claim 30 wherein said TRE is an AFP-TRE.

32. The method of claim 31 wherein said AFP-TRE is SEQ ID NO:__.

33. The method of claim 1, wherein the TRE is specific for bladder cells and the antineoplastic agent includes alkylating agents, antibiotics, immunomodulators, alkaloids, antimetabolites or hormone antagonists/antagonists and analogs.

34. The method of claim 33, wherein the antineoplastic agent includes cisplatin, thiotepa, mitomycin C, interferon alpha-2a, doxorubicin, mitoxantrone, bleomycin, paclitaxel, etoposide, gemcitabine, 5-fluorouracil, vinblastine, ifosfamide, methotrexate, goserelin, leuprolide, valrubicin, gallium nitrate, clyclophosphamide, vincristine, carboplatin, or docetaxel.

35. The method of claim 34 wherein said TRE is a uroplakin-TRE.

36. The method of claim 33 wherein said TRE is a uroplakin- TRE and said antineoplatic agent is doxorubicin.

37. The method of claim 1 wherein the TRE is CEA-TRE and the antineoplastic agent includes antibiotics, alkaloids, alkylating agents, antimetabolites and hormonal antagonists/agonists or analogs.

38. The method of claim 37, wherein the antineoplastic agent includes doxorubicin, mitoxantrone, epirubicin, mitomycin C, paclitaxel, 5-fluorouracil, thiotepa, goserelin, exemestane, methotrexate, irinotecan, edatrexate, letrozole, leuprolide, cisplatin, tamoxifen, anastrozole, prednisone, docetaxel, cyclophosphamide, or vinblastine.

39. The method of claim 1 wherein the TRE is tyrosinase-TRE and the antineoplastic agent includes alkylating agents, alkaloids, nitrosoureas and hormone antagonists/antagonists or analogs.

40. The method of claim 39 wherein the antineoplastic agent includes dacarbazine, carmustine, vinblastine, lomustine, tamoxifen, cisplatin, paclitaxel or docetaxel.

41. The method of claim 1 wherein a combination of antineoplastic agents is administered.

42. The method of claim 41 wherein said TRE is AFP and said combination includes doxorubicin/cisplatin, doxorubicin/mitomycin C, doxorubicin/mitoxantrone or doxorubicin/paclitaxel.

43. The method of claim 41 wherein said TRE includes PSA-TRE, PB-TRE and hKLK2-TRE and the combination includes estramustine/mitoxantrone,

estramustine/paclitaxel or estramustine/docetaxel.

44. The method of claim 41 wherein the TRE is a uroplakin-TRE and the combination includes M-VAC (methotrexate-vinblastine/doxorubicin/cyclophosphamide), CISCA (cyclophosphamide/doxorubicin/cisplatin), CMV (cisplatine/methotrexate/vinblatine), CAP (cyclophosphamide/doxorubicin/cisplatin), or MVMJ (methotrexate/vinblastine/mitoxantrone/carboplatin.

45. The method of claim 41, wherein the TRE is CEA and the combination includes levamisole/5-fluorouracil, leucovorin/5-fluorouracil, CAF (cyclophosphamide/doxorubicin/5-fluorouracil), CMF (clyclophosphamide/methotrexate, 5-fluorouracil), CNF (clycphosphamide/mitoxantrone/5-fluorouracil), FAC (5-fluorouracil/doxorubicin/cyclophosphamide), MF (methotrexate/5-fluorouracil/leucovorin), MV (mitoxantrone/vinblastine), CMFP (cyclophosphamide/methotrexate/5-fluorouracil/prednisone), or VATH (vinblastine/doxorubicin/thiotepa/fluoxymesterone).

46. The method of claim 41, wherein the TRE is tyrosinase and the combination includes DBPT (dacarbazine/cisplatin/carmustine/tamoxifen) or VDD (vinblastine/dacarbazine/cisplatin).

47. A method for suppressing tumor growth in an individual comprising: administering a target cell-specific adenoviral vector, said vector comprising an adenoviral gene essential for replication under transcriptional control of a target cell-specific-TRE, and administering an effective amount of an appropriate course of radiation therapy to the individual wherein wherein the amount of adenovirus vector and/or radiation administered is less than that known in the art to be effective for suppressing tumor growth when administered alone.

48. The method of claim 47 wherein said radiation includes external and internal radiation.

49. The method of claim 48 wherein said external radiation includes X-rays, gamma rays, alpha particles, beta particles, electrons, photons, neutrons, and other ionizing radiation.

50. The method of claim 48 wherein said internal radiation includes radioactive isotopes.

51. The method of claim 47 wherein said target cell specific TRE is a prostate specific TRE and said radiation is γ-irradiation.

52. A method for suppressing tumor growth in an individual comprising the following steps, in any order:

a) administering to the individual an effective amount of a target cell-specific adenoviral vector and an effective amount of at least one antineoplastic agent; and

b) administering an effective amount of an appropriate course of radiation therapy to the individual, wherein the amount of adenovirus vector and/or anitneoplastic agent and/or radiation administered will be less than that known in the art to be effective for suppressing tumor growth when administered alone.

53. The method of claim 52 further comprising c) administering to the individual an additional dose of adenoviral/antineoplastic agent or radiation as necessary to suppress tumor growth.

54. The method of claim 53 further comprising a delay between any of steps a), b) and c).

55. A composition comprising a target cell-specific adenoviral vector, said vector comprising an adenoviral gene essential for replication under transcriptional control of a target cell specific-TRE, and at least one antineoplastic

agent.

56. The composition of claim 55 further comprising a suitable pharmaceutical excipient.

57. The composition of claim 56 where the pharmaceutical excipient comprises saline solution, buffers, preservative, stabilizers, antiemetics or other adjuvant therapies.

58. A kit comprising the composition of claim 55 in an amount effective for suppressing tumor growth in an individual.

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